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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

|                       |   |                  |           |
|-----------------------|---|------------------|-----------|
| In re Application of: | Robert E. Wagner JR.                      |                  |           |
| Serial No.:           | 10/078,278                                | Group Art Unit:  | 1634      |
| Filed:                | February 20, 2002                         | Examiner:        | Bausch, S |
| For:                  | MUTATION DETECTION<br>USING MutS and RecA | Attorney Docket: | 007274-01 |

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

**DECLARATION  
37 C.F.R. 1.132**

Dear Sir:

This Declaration is made by Dr. Robert E. Wagner, Jr., inventor of the present application. This Declaration is submitted in conjunction with an amendment and response to the office action mailed from the USPTO on November 30, 2005.

I, Robert E. Wagner, state and declare as follows:

1. I am an employee of Gene Check Inc. and the inventor of the present invention.
2. As inventor of the present invention, I am highly familiar with the art pertaining to MutS proteins.
3. At the time the present invention was filed, it was understood by one of skill in the art that the ability of MutS proteins to bind mismatches is complex and greatly

affected by: (1) the nature of the mismatch, (2) the state of the mismatch, i.e., intra-helical vs extrahelical, and (3) even the surrounding nucleotide sequence.

4. In support of this position, the following references are attached:

- i. Dohet et al. 1985, Proc. Natl. Acad. Sci. Vol. 82 pp 503-505.
- ii. Su et al. 1988, J. Biol. Chem. Vol. 263, No. 14 pp 6829-6835
- iii. Fazakerley et al. 1986, EMBO Journal Vol. 5, No. 13 pp 3697-3703
- iv. Jones et al. 1987, Genetics 115:605-610

5. As one of skill in the art, I assert that the enclosed references may be summarized as follows:

i. In Dohet et al., results are presented from experiments using *in vivo* constructed lambda heteroduplexes containing each of the eight possible mismatches. The heteroduplexes were transfected into *E. coli* and repair monitored. The finding is that all mismatches are not repaired equally, i.e. MutS does not see all mismatches equally.

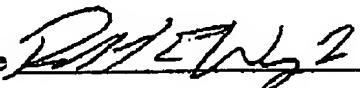
ii. In Su et al., the authors used an *in vitro* repair system and found results similar to Dohet et al.

iii. Fazakerley et al. used NMR to study MutS binding to mismatches. It was found that MutS recognizes mismatches only when they are intrahelical and that "looped out" configurations are not seen by MutS.

iv. Jones et al. showed that the ease of recognition of mismatches by MutS also depends on surrounding base composition.

6. Accordingly, one of skill in the art would conclude that the ability of MutS to bind mismatches, which is highly variable even under "normal" conditions would be unpredictable under circumstances where the structure of the DNA has been altered (two strand duplex vs. three strand D-loop or triple helix).

7. I hereby declare that all statements made herein of my own are true and that all statements made on information and belief are believed to be true; and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the subject application or any patent issuing thereon.

Inventor's Signature  Dated: May 1, 2006

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